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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 6537
Title: Perspectives of new biomarkers in gastric cancer: diagnostic and prognostic applications
Reviewer code: 02546675
Science editor: Ma, Ya-Juan
Date sent for review: 2013-10-24 09:24
Date reviewed: 2013-10-25 16:55

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[Y] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[Y] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[ ]Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[Y] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS
The article reviewed a panel of molecular markers which may be used in a diagnostic and prognostic manner for gastric cancer. The authors compared several markers including genetic, epigenetic and proteomic ones for discussing the pros and cons of each type of marker, and the comparisons may help to improve the clinical practice. Also, the clear logical frame used in this article make it understandable. However, some sentences should be refined before publication.

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ESPS Peer-review Report
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[Y] Accept
[ ] Grade B (Very good)	[Y] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[Y] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[ ]Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[ ] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS

To the Authors, 04.12.2013

This Topic Highlight article entitled "Perspectives of new biomarkers in gastric cancer: diagnostic and prognostic applications" (Manuscript Number: 6537) reviews the biomarkers of gastric cancer in terms of diagnosis and prognosis with a broad spectrum of biological samples and detection methods, including genetic, epigenetic and proteomic approaches. Gastric carcinogenesis is a multifactorial process, in which infection with Helicobacter pylori, environmental factors and genetic susceptibility factors play major roles. In this review, authors summarize the recent genetic, epigenetic and proteomic approaches of gastric cancer successfully.
Yours sincerely.

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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[Y] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[Y]Rejection
[Y] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[ ] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS

The current article presents data concerning an interesting problem, but there are a lot of points inadequate. In the Introduction part it is important to introduce the reader in the problematic and potential of biomarkers. The access to such an important but for clinicians and readers often theoretical subject has to be simplified by a sentence like: E.g. "The aim in detecting new biomarkers for gastric cancer is amongst others to facilitate the diagnosis of GC with non-invasive but specific diagnostic tools and enable tailored therapies." The different parts of the review could profit from a reconstruction and more precise analysis of current data. In parts the review is to long but significant details are missed. Examples for improving the paper are presented in the following, divided into the sections appropriate to the structure of the manuscript. 1.) Genomic instability HER2 overexpression, appearing in 6 to 35% of gastric carcinomas and overexpression was associated with poorer clinical outcome. HER2 overexpression varies significantly with the histological subtype. Approximately 34% of the intestinal type, 6% of the diffuse forms and 20% mixed type according to Lauren`s classification. HER2 overexpression also varies regarding the primary localization of the gastric carcinoma. These are examples of essential and basic information concerning HER2. The prognostic value of overexpression or HER2 gene amplification in gastric cancer information is not questionable (as maintained in the manuscript) but of great value e.g. Trastuzumab (TOGA-trial) / Lapatinib (GastroLap-study). Surely further studies are needed to assess the prognostic significance of HER2 positivity, but the most clinical application of HER2 status is the management of advanced or metastatic GC, so HER2 testing is according to the NCCN- Guidelines recommended for patients with inoperable locally advanced, recurrent and metastatic adenocarcinoma of the stomach. 2.) Mutations and polymorphisms The role of CDH1 and p53 is well described in the literature. But

nevertheless the practical aspects of these markers are not well described in the part of "mutations and polymorphisms" in this manuscript. Therefore the IL`s (Interleukin) are presented in an unstructured manner. The IL`s should be demonstrated in more specific way or be omitted. A more practical aspect could be, e.g.: Germ line mutations of CDH1 are associated with the development of diffuse- type gastric cancer . To mention the role of prophylactic gastrectomy seems to be important. There are still inconsistent data nowadays showing studies of CDH1 positive patients without cancer in the gastrectomy specimen and the relation between quantities of tissue blocks needed to identify foci of gastric cancer. In such a review the proofed markers should be presented in a more clinical context so that clinicians will be aware that such genetic techniques are not only theoretically tools and the use and understanding in the daily routine will be simplified. 3.) Proteomics The diagnostic and prognostic aspects of proteomic based techniques in cancer biology are huge therefore in a review it seems to be important not to try to mention as much proteomics as possible. It is essential to show the reader what is relevant and better up to date and relevant in the field. Even for readers performing clinical medicine in gastroenterology or gastrointestinal surgery. In the "Proteomics" part it is said:" …However, the sensitivity and specificity of these markers are not sufficient for the diagnosis of GC and therefore should not be used in routine clinical practice [89,90]…" This is not correct. It is important to know the limitation of a method and e.g. what is the aim when CA 72-4 or CEA is analyzed. These are markers proven in the clinical routine. This kind of verbalization has to be changed. 4.) Epigenetics (Mi RNA) The Micro- RNA part should be completely revised and presented more preci

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ESPS Peer-review Report
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[Y] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
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[ ] Grade E (Poor)		[ ] Existed	[Y] Major revision
		[ ] No records	

COMMENTS TO AUTHORS

This study is a very comprehensive review about genetic, proteomic and epigenetic markers of gastric cancer. We suggest a few remarks: Abstract: line 4: the word "approach" should be substituted with "intent" or "purpose". Genetic markers Genomic instability: line 14: the word "used" should be cancelled. Mutations and polymorphisms: paragraph 7: the word "used" should be avoided in this case. Proteomics: paragraph 6: the word "applied" should be substituted with a more correct word. In addition, greater emphasis should be used to express the practical implications of the various markers, providing sensibility, specificity, measurements, and on what kind of sample it should be performed; e.g. X is an invasive/non-invasive marker, measured on blood/biopsy/surgical specimen that can be used to diagnose or that can be adopted to express a prognostic judgment about... with a sensibility of … and specificity of …). Moreover, tables could be adopted to compare or summarize various markers and their characteristics.

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Title: Perspectives of new biomarkers in gastric cancer: diagnostic and prognostic applications
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Science editor: Ma, Ya-Juan
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[Y] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[ ]Rejection
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Science editor: Ma, Ya-Juan
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[Y] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[Y] Grade C: a great deal of language polishing	[ ] No records	[ ]Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[Y] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS

The authors present a brief yet comprehensive review of biomarkers with potential diagnostic or prognostic significance in gastric cancer, highlighting the importance of patient ethnicity in genetic biomarkers. The review is logically organized into three sections covering genetic, proteomic, and epigenetic biomarkers. The subject is important, because there is widespread recognition that biomarkers can play a role in the management of gastric cancer, yet persistent confusion regarding their optimal clinical use. I have a few concerns. A) Throughout the manuscript, the language requires polishing. For example, the title should be "Perspectives on..." rather than "Perspectives of..." More specific examples, drawn from the introduction alone: 1) "after lung cancer" not "together with lung cancer" 2) "imaging methods" not "image methods" 3) "high mortality" not "elevated death incidence" 4) "prediction of therapeutic response" not "predict therapeutic response" Similar errors persist throughout the manuscript and interfere with an otherwise clear presentation of the ideas and concepts. B) In the United States, the most widely used gastric cancer biomarker is CA 19-9. Can the authors add a few sentences to discuss the results of specific human studies addressing the validity of this marker? C) In the abstract and elsewhere in the manuscript, the authors write that "use of a panel of several markers... should be the best alternative for clinical practice." However, the authors have not provided evidence that use of biomarkers improves gastric cancer-related outcomes. If there is no evidence that use of biomarkers improves outcomes, how can we justify the expense of these tests? Please address this point.

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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[Y] Grade B (Very good)	[Y] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[ ]Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[Y] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS
This is a very thorough manuscript detailing the molecular diagnostics and prognostics in gastric cancer. I have the following comments: 1. I think there are too many references. Could these be cut down? 2. The tables focus only on MiRNA. Could other genetic mutations (SNPs, HER2, proteomics, etc…) be incorporated into an additional graph or table? Would be nice to have at least one more 3. I think the translational impact of the review would be stronger if there were a couple paragraphs in the discussion about therapeutics related to these findings. Even if we don't have targeted agents for trials currently, could the authors speculate about how these molecular findings could be targeted in the future?